Filed: March 30, 2001

Page 2

Amendments to the Claims

Listing of Claims

1-73. (Canceled)

- 74. (Currently Amended) A method for sequencing a DNA which comprises:
 - treating the DNA with a mixture comprising (a) primer, a DNA polymerase, oligonucleotide four different deoxynucleotides, and four different labeled dideoxynucleotides, under conditions permitting a deoxynucleotide or a labeled dideoxynucleotide or both to be incorporated into a DNA sequencing fragment, wherein each different deoxynucleotide and each different labeled dideoxynucleotide is complementary to one of the four nucleotides present in the DNA, wherein each labeled dideoxynucleotide comprises a moiety attached via a chemical linker dideoxynucleotide[[;]], and wherein each of the four different labeled dideoxynucleotides has a molecular weight which can be distinguished from the molecular weight of the other three labeled dideoxynucleotides using mass spectrometry;
 - generating a plurality of DNA sequencing fragments (b) having different lengths that are terminated with the labeled dideoxynucleotides to generate a so as labeled DNA plurality οf different fragments, wherein each DNA sequencing fragment has a 3' end and the chemical moiety is attached via the linker to the 3' end of the DNA sequencing fragment;

Filed: March 30, 2001

Page 3

- contacting the labeled DNA sequencing fragments with a (c) surface coated with a compound that specifically interacts with the chemical moiety attached via the linker to the 3' end of the DNA sequencing fragments, thereby capturing the labeled DNA sequencing fragments on the surface compound, wherein the contacting is performed in a system comprising (i) a chip comprising a plurality of channels whose surfaces is are coated with a the compound that specifically interacts with channel wherein <u>eac</u>h chemical moiety, the comprises two ends, the first of which is connected via a glass capillary to, (ii) a first well of a plurality of wells each suitable for holding a sample and the second of which is connected to a second well of the plurality of wells, (iii) a connection between one end of the channel and a first well, and a connection between the other end of the channel and a second well, and (ivii) a means for moving the sample by pressure multiple times between wells through the channels between wells, wherein the sample is moved by pressure multiple times between wells through the channels;
- (d) washing the surfaces to remove non-bound components;
- (e) treating the labeled DNA sequencing fragments so as to release the labeled DNA sequencing fragments from the surfaces; and
- (f) determining the difference in molecular weight between different labeled DNA sequencing fragments which are represented as adjacent peaks on a mass spectra of the labeled DNA sequencing fragments produced using

Filed: March 30, 2001

Page 4

matrix-assisted laser desorption/ionization time-offlight mass spectrometry, so as to sequence the DNA; wherein either (i) the labeled dideoxynucleotides are biotinylated dideoxynucleotides selected from the group consisting of Applicant: Jingyue Ju et al. U.S. Serial No.: 09/823,181 Filed: March 30, 2001

Page 5

$$\begin{array}{c|c} & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

Filed: March 30, 2001

Page 6

where ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides; or

Filed: March 30, 2001

Page 7

(ii) the linker is selected from the group consisting of

and

75. (Currently Amended) The method of claim 74, wherein the interaction between the chemical moiety attached via the linker to the DNA sequencing fragment and the compound on the surfaces is selected from the group consisting of a biotin-streptavidin interaction, a phenylboronic acid-salicylhydroxamic acid interaction, and an antigen-antibody

Filed: March 30, 2001

Page 8

interaction.

- 76. (Previously Presented) The method of claim 74, wherein the dideoxynucleotide comprises a cytosine or a thymine with a 5-position, or an adenine or a guanine with a 7-position, and the linker is attached to the 5-position of cytosine or thymine or to the 7-position of adenine or guanine.
- 77. (Previously Presented) The method of claim 74, wherein the linker comprises a derivative of 4-aminomethyl benzoic acid containing a carbon-carbon triple bond.
- 78. (Previously Presented) The method of claim 77, wherein the linker comprises one or more fluorine atoms.
- 79. (Currently Amended) The method of claim 74, wherein the step of releasing the DNA sequencing fragments from the surfaces comprises disrupting the interaction between the chemical moiety attached via the linker to the DNA sequencing fragments and the compound on the surfaces.
- 80. (Previously Presented) The method of claim 79, wherein the interaction is disrupted by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.
- 81. (Currently Amended) The method of claim 74, wherein the step of releasing the DNA sequencing fragments from the surfaces comprises cleaving the linker.

Filed: March 30, 2001

Page 9

- 82. (Previously Presented) The method of claim 81, where the linker is cleaved by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.
- 83. (Previously Presented) The method of claim 82, wherein the linker is cleaved by light.
- 84. (Previously Presented) The method of claim 74, wherein the linker is selected from the group consisting of

and

Filed: March 30, 2001

Page 10

- 85. (Previously Presented) The method of claim 74, wherein a plurality of different linkers is used to increase mass separation between different labeled DNA sequencing fragments and thereby increase mass spectrometry resolution.
- 86. (Currently Amemded) The method of claim 74, wherein the chemical moiety comprises biotin, the labeled dideoxynucleotides are biotinylated dideoxynucleotides, the labeled DNA sequencing fragments are biotinylated DNA sequencing fragments, and the surfaces is a are streptavidin-coated solid surface.

Filed: March 30, 2001

Page 11

87. (Previously Presented) The method of claim 86, wherein the biotinylated dideoxynucleotides are selected from the group consisting of:

wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.

Filed: March 30, 2001

Page 12

88. (Previously Presented) The method of claim 87, wherein the biotinylated dideoxynucleotides are selected from the group consisting of:

Filed: March 30, 2001

Page 13

89. (Previously Presented) The method of claim 86, wherein the biotinylated dideoxynucleotides are selected from the group consisting of:

wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.

Filed: March 30, 2001

Page 14

90. (Previously Presented) The method of claim 89, wherein the biotinylated dideoxynucleotides are selected from the group consisting of:

91-92. (Canceled).